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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/524,787	09/23/2005	Lea Eisenbach	EISENBACH4A	8693

1444 7590 03/18/2008

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EXAMINER	
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ART UNIT	PAPER NUMBER
1643	

MAIL DATE	DELIVERY MODE
03/18/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/524,787	EISENBACH ET AL.	
	Examiner	Art Unit	
	LYNN BRISTOL	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 January 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-7,9,12-17,21-33,35-39 and 43-62* is/are pending in the application.

4a) Of the above claim(s) *24-29,46-58,60 and 61* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 3-6, 9, 12-17, 21-23, 30-33, 35-39, 43-45, 59 and 62* is/are rejected.

7)☒ Claim(s) *7* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1)☒ Notice of References Cited (PTO-892)

2)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)

3)☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.

4)☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.

5)☐ Notice of Informal Patent Application

6)☐ Other: _____.

DETAILED ACTION

1. Claims 1, 3-7, 9 and 12-17, 21-33, 35-39 and 43-62 are all the pending claims for this application.

2. Claims 18-20, 34 and 40-42 were cancelled, Claims 1, 15-17, 21-23, 30-33, 35-39 and 43-45 were amended and new Claim 62 was added in the Response of 1/10/08.

3. Claims 24-29, 46-58, 60 and 61 are withdrawn from examination.

4. Claims 1, 3-7, 9, 12-17, 21-23, 30-33, 35-39, 43-45, 59 and 62 are all the claims under examination.

5. Applicants amendments to the claims have necessitated new grounds for rejection.

Withdrawl of Objections

Specification

6. The objection to the specification for failing to provide a sequence identifier for the following sequence pursuant to 37 CFR 1.821 (c) and/or (d), PI-P2-P3-P4-P5-P6-P7-P8-P9 (see p. 30), is withdrawn.

Applicants' comments on p. 10 of the Response of 1/10/08 have been carefully considered and are found persuasive.

Withdrawal of Rejections

Enablement (1)

7. The rejection of Claims 16-20 and 31-42 under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement for pharmaceutical compositions with an intended use for treating or inhibiting the development of colon cancer with the inventive MHC-class I binding, CTL-inducing peptides, and vaccine compositions and cellular vaccine compositions is withdrawn.

The rejection is moot for cancelled Claims 18-20, 34 and 40-42. The rejection is obviated for Claims 16-17, 31-33 and 35-39 in view of the amendment of the claims to delete the recitation "pharmaceutical."

Applicants' comments on p. 14 of the Response of 1/10/08 are acknowledged.

The rejection of Claims 15, 21-23, 30 and 43-45 is maintained as discussed below.

8. The rejection of Claim 7 under 35 U.S.C. 112, first paragraph, in lacking enablement for any peptide isolated from any protein expressed by any polynucleotide from a human colon carcinoma cell where the peptide has the ability to bind MHC Class I *and* elicit a peptide-specific CTL response and where the peptide optionally includes at least one non-natural modification is withdrawn.

Claim 7 is drawn to the protein encoded by human 1-8D gene and is shown in the specification (Tables 2 and 3) to meet the requirements of Claim 1.

Claim Rejections - 35 USC § 102

9. The rejection of Claims 1, 3, 4, 9 and 12-14 under 35 U.S.C. 102(e) as being anticipated by Afar et al. (US2005063975, with priority to USPN 6,833,438 and USPN 6,329,503; all of which are cited in the PTO form 892 of 4/12/07) is withdrawn.

The amendment of Claim 1 to recite the negative limitation "with the proviso that the protein is not a six transmembrane epithelial antigen of the prostate (STEAP) protein" meets and overcomes the rejection.

Applicants' comments on p. 16 of the Response of 1/10/08 are acknowledged.

Rejections Maintained

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Enablement 1

10. The rejection of Claims 15, 21-23, 30 and 43-45 under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement for an intended use for treating or inhibiting the development of colon cancer with the inventive MHC-class I binding, CTL-inducing peptides presented as a "cell composition" is maintained.

Applicants' allegations on p. 14 of the Response of 1/10/08 have been considered but are not found persuasive. Applicants allege that in amending the claims

to replace the limitation "cellular vaccine composition" with "a cell composition" that the claims are fully enabled (or would otherwise remove the requirement that the composition is a vaccine with intended prophylactic properties).

The examiner submits that in requiring the composition (generic Claims 15 and 30) to comprise a "cell composition" comprising "an antigen presenting cell which presents said at least one peptide", Applicants are required to show with a reasonable number of examples that the peptide(s) in fact could be presented by an APC in order to accomplish the required elicitation of a CTL response. The amendment to delete "vaccine" excludes the requirement that the composition is prophylactic, but the compositions still comprise a literal functional component, the APC, which is a) genetically modified with a polynucleotide encoding the TAA peptide, b) loaded with at least one polynucleotide encoding the TAA peptide, c) loaded with TAA peptides *and/or* d) loaded with polypeptides comprising TAA peptides. The claims embrace recombinant APCs having the ability to express and present the TAA peptide for CTL induction. Applicants' specification does not demonstrate any example of a recombinant APC showing all of the instant claimed characteristics of the compositions. Accordingly, the composition still reads on an intended use where APC is applied in a manner (in vitro or in vivo) to elicit the CTL response that is not fully enabled by the specification at the time of filing.

Enablement 2

11. The rejection of Claims 1, 3, 4, 9, 12-14 (and Claims 15-17, 21-23, 30-33, 35-39, 43-45 and 62) under 35 U.S.C. 112, first paragraph, in lacking enablement for a peptide isolated from a protein expressed by any polynucleotide from a human colon carcinoma cell where the peptide has the ability to bind MHC Class I *and* elicit a peptide-specific CTL response and where the peptide optionally includes at least one non-natural modification is maintained (Claims 1, 3-6, 9, 12-17, 21-23 and 62).

Claims 30-33, 35-39, and 43-45 are added to the rejection because the claims are not enabled for just any peptide isolated from a 1-8D protein or a 1-8D protein expressed by a polynucleotide from a human colon carcinoma cell where the peptide has the ability to bind MHC Class I *and* elicit a peptide-specific CTL response and where the peptide optionally includes at least one non-natural.

A) On pp. 11-13 of the Response of 1/10/08 Applicants allege the claims are fully enabled for the breadth of peptides because: 26 examples of peptides from colorectal genes are shown in Table 2, three peptides derived from 1-8D interferon induced transmembrane protein 2 (SEQ ID NO:59) are shown to be antigenic and immunogenic in HHD mouse model and the working models in the specification provide "sufficient guidance for one of skill in the art to determine other TAA peptides of a protein encoded by a polynucleotide overexpressed in human colon carcinoma cells without undue experimentation. Applicants then assert that the literature provided as extrinsic support show peptides similarly identified without undue experimentation.

The examiner submits that Applicants specification as originally filed does not support the breadth of TAA peptides meeting all of the limitations of the instant claims. The overexpressed proteins from colon carcinoma were screened for putative HLA-A2.1 restricted peptides using the "independent binding of individual peptide side-chains" software (Parker et al., 1994). HLA-A2.1-restricted peptides from the selected genes were selected according to its consensus binding motifs are shown in Table 2. Of the 26 peptides, 7 were shown to be immunogenic in vivo and 3 peptides were from human 1-8D interferon induced transmembrane protein 2 (SEQ ID NO:59). Not all of the putative peptides in Table 2 were antigenic under assay conditions, only 7 were immunogenic, and 3 of the 7 are all from the same protein (human 1-8D interferon induced transmembrane protein 2). Applicants own data in the specification are dispositive to the assertion that just any peptide can be designed and that would predictably bind MHC to promote a CTL response in vitro much less in vivo.

The reference copies provided with the Response are acknowledged but Applicants have not provided any explanation as to how the references are relevant to the instant claimed peptides derived from human colon carcinoma TAA. For example, are any of the reference TAA-derived peptides also described in the specification as overexpressed, colon cancer-derived TAAs?

Machlenkin describes peptides from PAP-3 ((Can. Res. 65:6435-6442 (2005) and (Can. Immunol. Immunother.56:217-226 (2007)) in prostate cancer and peptides from STEAP from prostate cancer (Can. Res. 65:6435-6442 (2005)). Applicants' claims specifically exclude STEAP-derived peptides so the reference is irrelevant. Applicants'

specification teaches "The oldest discovered **prostate-restricted antigens** have included prostate-specific antigen (PSA), prostate-specific membrane antigen (PSMA) and prostatic acid phosphatase (PAP)" [0140]. How is PAP-3 related to a human colon carcinoma TAA and what is the relevancy of the reference?

Bar-Haim (Br. J. Can. 91:398-407 (2004) describes peptides from MAGE-A8 protein in bladder cancer. Applicants' specification does not define much less mention MAGE-A8 being a colon cancer TAA. Bar-Haim describes MAGE-A8 protein expression occurring in 44% of colorectal carcinomas but not in any normal colon samples (p. 398, Col. 2, ¶3). Thus MAGE-A8 protein does not even meet the requirements of the claims, which is that the protein is overexpressed, implying that some basal level of expression would need to occur in a normal cell. What is the relevancy of the reference?

Carmon (Int. J. Can. 85:391-397 (2000)) describes peptides from MUC1 protein in breast cancer. Applicants' specification does not define much less mention MUC1 being an overexpressed colon cancer TAA. What is the relevancy of the reference?

Carmon (J. Clin. Invest. 110:453-462 (2002) describes peptides from BA46 protein in breast cancer. Applicants' specification does not define much less mention MUC1 being an overexpressed colon cancer TAA. What is the relevancy of the reference?

Stepensky (Clin. Exp. Immunol. 143:139-149 (2005) describes peptides from MUC-1 in lung carcinoma. Applicants' specification does not define much less mention MUC1 being an overexpressed colon cancer TAA. What is the relevancy of the reference?

Applicants have not cited any references that are enabling for the scope of peptides encompassed by the claims at the time of application filing. Applicants have demonstrated that only a small percentage of colon carcinoma TAA-derived peptides modeled from the software program were immunogenic thus one of skill in the art could not reliably and predictably use peptides designed from the software and consensus binding motifs without further experimentation to determine which peptides could bind MHC and elicit a CTL response. The claims further encompass modified peptides, thus the claim scope far exceeds what Applicants have actually demonstrated by working example in the specification or what was known in the art for colon carcinoma-derived immunogenic peptide at the time of filing.

B) On p. 13 of the Response of 1/10/08 Applicants have urged the Office to consider "post-filing experimental results obtained in the laboratory of the present inventors to show that some amino acid modifications of 1-8D peptide 3-7 and all modifications of 1-8D peptide 3-5 induced a CTL response."

The examiner respectfully submits that the data has not been considered because of the improper presentation under MPEP 2162.05 and 37 CFR 1.132:

> "§ 1.132 Affidavits or declarations traversing rejections or objections. When any claim of an application or a patent under reexamination is rejected or objected to, any evidence submitted to traverse the rejection or objection on a basis not otherwise provided for must be by way of an oath or declaration under this section. [48 FR 2713, Jan. 20, 1983, effective Feb. 27, 1983; revised, 61 FR 42790, Aug. 19, 1996, effective Sept. 23, 1996; revised, 65 FR 54604, Sept. 8, 2000, effective Sept. 8, 2000; revised 65 FR 57024, Sept. 20, 2000, effective Nov. 29, 2000]."

Applicants are invited to resubmit the new data in the form of 1.132 Declaration signed by one of the named inventors and to identify literal support in the original specification for the examples of the modified peptides in order to avoid raising any issues of new matter. Alternatively, Applicants are invited to file a C-I-P application containing the new data.

C) On pp. 13-14 of the Response, Applicants allege that because the specification describes numerous prophetic or hypothetical examples of non-natural modifications to peptides using positions P1-P9 as guidance, that one of skill in the art could design and model TAA peptides of 8 to 10 amino acid residues from any colon-cancer associated TAA.

The examiner submits that the 7 operative peptides meeting the claim limitations filed in the original specification were not modified from the corresponding stretch of amino acid residues in the corresponding colon cancer protein. All of them corresponded to the native sequence structure from the native protein. Applicants' new data allegedly describes examples of modified peptides for the immunogenic peptides 3-5 and 3-7 from 1-8D interferon inducible protein 2, however, that information has not been considered for the reasons set forth above. Applicants are invited to file the data under a 1.132 Declaration to advance the examination proceeding.

Finally, Applicants specification in Table 2 teaches several non-operative embodiments for peptides which were designed to correspond to native protein structures, and Applicants are now urging the Office to believe that one could further

modify a peptide of unpredictable immunogenicity to create an immunogenic, modified peptide absent a proper showing of expected results.

Enablement 3

12. The rejection of Claims 5, 6 and 59 under 35 U.S.C. 112, first paragraph, in lacking enablement for any immunogenic peptide derived from the protein encoded by the nucleotide of SEQ ID NO:58 (human 1-8D interferon inducible protein 2) or encoded by the nucleotide of SEQ ID NO: 60 (human 1-8D interferon inducible protein 2 polymorphism) is maintained.

Applicants' allegations on pp. 14-17 of the Response of 1/10/08 have been considered but are not found persuasive. Applicants allege there is very little difference between the nucleotide sequence of SEQ ID NO: 59 for human 1-8D interferon inducible protein 2 and the nucleotide sequence of SEQ ID NO:60 or the encoded protein thereof (SEQ ID NO: 61) for the polymorphic human 1-8D interferon inducible protein 2 so that the 3 peptides shown in the specification to bind MHC and elicit CTLs (from the protein encoded by SEQ ID NO: 59) would be the same as the peptides from the protein of SEQ ID NO:61 at inducing the response. Further, because the peptide domains for the 3 peptides fall outside of the polymorphic residue(s) of SEQ ID NO:60 and 61, the same 3 immunogenic peptides would occur in the structure of the protein of SEQ ID NO:61 as the protein encoded by the nucleotide of SEQ ID NO:58.

The examiner respectfully submits that the claim scope is not limited to any of the 3 peptides shown in the specification but to any peptide falling within the structure of the

protein encoded by the nucleotide of SEQ ID NO:58 (human 1-8D interferon inducible protein 2) or encoded by the nucleotide of SEQ ID NO: 60 (human 1-8D interferon inducible protein 2 polymorphism). The proteins are considered to be separate and distinct because they have different sequence structures.

New Grounds for Rejection

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Written Description

13. Claims 1, 3-7, 9, 12-17, 21-23, and 62 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 1, 3-7, 9, 12-17, 21-23, and 62 are drawn to an isolated TAA peptide of 8-10 amino acid residues which promotes binding to MHC class, elicits a CTL response, is obtained from a protein overexpressed in human colon cancer, and "*is not a six transmembrane epithelial antigen of the prostate (STEAP) protein*".

The use of a negative limitation is used to define the invention in terms of what it is not, rather than distinctly and particularly claiming a specific peptide or class of

peptides that meet the claim requirements and that is supported (and enabled) in the specification. Under MPEP 2173.05(i) "Any negative limitation or exclusionary proviso must have basis in the original disclosure."

The specification defines several putative antigenic peptides derived from proteins associated with human colon carcinoma in Table 2, antigenic peptides in Table 3 and immunogenic peptides (underlined peptides) in Table 3, but does not provide specific written support for the negative limitation "*is not a six transmembrane epithelial antigen of the prostate (STEAP) protein*." Applicants have not and cannot identify per se support in the specification for the negative limitation as presently recited. Applicants are requested to identify the exact page, paragraph and line where the negative proviso is taught in the specification (MPEP 2173.05(i)). Further, by excluding the peptide(s) of the STEAP class of proteins, the claims encompass myriad other peptides that are not fully supported or enabled by the record evidence. One skilled in the art would conclude that Applicants were not in possession of the invention for any isolated TAA peptide of 8-10 amino acid residues which promotes binding to MHC class, elicits a CTL response, is obtained from a protein overexpressed in human colon cancer, and "*is not a six transmembrane epithelial antigen of the prostate (STEAP) protein*" when instead the only other species of peptides, distinctly and particularly described in the specification are the peptides in Tables 2 and 3.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

14. Claims 30-32 are rejected under 35 U.S.C. 102(e) as being anticipated by Matsuzaki et al. (US 20030092037; published 5/15/03; filed 7/18/02).

Claims 30-32 are interpreted as being drawn to a composition comprising a pharmaceutically acceptable carrier or diluent or excipient and a member, where the member is a TAA encoded by human 1-8D interferon inducible gene (Claim 30, element (A) and Claim 31) and the TAA comprises the amino acid sequence of SEQ ID NO: 59 (Claim 32).

Matsuzaki teaches pharmaceutical compositions comprising as the active ingredient a protein having 100% sequence identify to the protein of SEQ ID NO: 59 of instant Claim 32 and which may be combined with other active ingredients or inactive ingredients (e.g., conventional pharmaceutically acceptable carriers or diluents such as immunogenic adjuvants) and physiologically non-toxic stabilizers and excipients [0137]. The sequence search alignment for the protein of Matsuzaki and the protein of SEQ ID NO:59 is attached.

The claimed member appears to be the same as the prior art protein, absent a showing of unobvious differences. The office does not have the facilities and resources to provide the factual evidence needed in order to establish that the product of the prior art does not possess the same material, structural and functional characteristics of the claimed product. In the absence of evidence to the contrary, the burden is on the applicant to prove that the claimed product is different from those taught by the prior art and to establish patentable differences. See In re Best 562F.2d 1252, 195 USPQ 430 (CCPA 1977) and Ex parte Gray 10 USPQ 2d 1922 (PTO Bd. Pat. App. & Int. 1989).

15. Claims 30 and 31 are rejected under 35 U.S.C. 102(e) as being anticipated by Berger et al. (US 20030148410; published August 7, 2003; priority to U.S. Provisional Application No. 60/339971, filed December 10, 2001).

The interpretation of Claims 30 and 31 are discussed supra.

Berger discloses biomarker proteins overexpressed in colon cancer cells compared to normal colon cancer cells comprising 1-8D interferon induced transmembrane protein 2 (IFITM2) (Table 1), for use in compositions [0105] with a pharmaceutically acceptable carrier [0219] or diluent [0242].

Conclusion

16. No claims are allowed.

17. Claim 7 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims. The closest prior art is the full length protein for 1-8D interferon inducible protein (Reid et al. PNAS 86:840-844 (1989)) comprising the amino acid sequence corresponding to the amino acid sequence of the 3-7 peptide of SEQ ID NO: 27 (see attached sequence search alignment for SEQ ID NO: 27).

18. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lynn Bristol whose telephone number is 571-272-6883. The examiner can normally be reached on 8:00-4:00, Monday through Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on 571-272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

LAB

/Larry R. Helms/

Supervisory Patent Examiner, Art Unit 1643